amplification occurs in over 50% of human breast cancers. (Saint-Ruf et al., supra.) A variety of oncogenes have been found to be amplified in human malignancies. Examples of the amplification of cellular oncogenes in human tumors are shown in Table 1 below.

TABLE 1

Amplified Gene	Tumor	Degree of Amplification
c-myc	Promyelocytic leukemia, cell line, HL60	20x
	Small-cell lung carcinoma cell lines	5-30x
N-myc	Primary neuroblastomas (stages III and IV) and neuroblastoma cell lines,	5-1000x
	Retinoblastoma cell line and primary tumors,	10-200x
	Small-cell lung carcinoma cell lines and tumors	50x
L-myc	Small-cell lung carcinoma cell lines and tumors	10-20x
c-myb	Acute myeloid leukemia	5-10x
	Colon carcinoma cell lines	10x
c-erbb	Epidermoid carcinoma cell	30x
	Primary gliomas	
c-K-ras-2	Primarycarcinomas of lung colon, bladder, and rectum	4-20x
N-ras	Mammary carcinoma cell line	5-10x

a1

[On page 6, lines 1-5, please replace with the following paragraph:]

a2 For example, as disclosed in U.S. Patent No. 5,846,749, the amplification of the Her-2 gene has been linked to invasive breast cancer phenotypes. In a study of node-negative invasive breast carcinomas, the degree of HER-2/neu gene amplification was determined by Southern blot analysis

Q2 of EcoRI digested tumor tissue and the relative amount of HER-2/neu mRNA was determined by Northern hybridization of total RNA.

[On page 8, line 22 to page 9, line 9, please replace with the following paragraph:]

Restriction fragment length polymorphism (RFLP) studies have indicated that several tumor types have frequently lost heterozygosity at 13q, suggesting that one of the Rb-1 gene alleles has been lost due to a gross chromosomal deletion (Bowcock et al., Am. J. Hum. Genet., 46: 12 (1990)). The deletion of the short arm of chromosome 3 has been associated with several cancers, for Q3 example, small cell lung cancer, renal and ovarian cancers; it has been postulated that one or more putative tumor suppressor genes is or are located in the p region of chromosome 3 (ch. 3p) (Minna et al., Symposia on Quantitative Biology, Vol. LI: 843-853 (SCH Lab 1986); Cohen et al., N. Eng. J. Med., 301: 592-595 (1979); Bergerham et al., Cancer Res., 49: 13901396 (1989); Whang-Peng et al., Can. Genet. Cytogenet., II: 91-106 (1984; and Trent et al., Can. Genet. Cytogenet., 14: 153-161 (1985)).

[On page 10, line 18, to page 11, line 4, please replace with the following paragraph:]

Clinical classification utilizing the TNM system is based on evidence acquired before primary treatment. Pathologic classification includes the evidence acquired before treatment, as well Q4 as evidence acquired from surgery. The three components, T, M and N, are assessed. The use of numerical subsets of the TNM components indicates the progressive extent of the malignant disease. Any of the T, N, or M classifications can be divided into subgroups for testing. The TNM components can then be evaluated to determine the stage grouping (I-IV) of growth for the patient's cancer. The clinical stage is used as a guide to the selection of primary therapy, usually a form of

Q4 surgery to remove the cancerous lesions. The pathologic stage can also be used as a guide for adjuvant therapy (chemotherapy), prognosis, and reporting end results.

On page 15, line 13 to page 16, line 17, please replace with the following paragraphs:

Other lysophospholipids associated with various conditions include lysophosphatidyl serine (LPS), lysophosphatidyl ethanolamine (LPE), lysophosphatidyl glycerol (LPG) and lysophosphatidyl inositol (LPI). Activated platelets secrete two kinds of phospholipase: sPLA2 and PS-PLA1. sPLA2 is reported to be elevated in inflammatory reactions and inhibition of this enzyme reduced

Q5 inflammation. PS-PLA1 hydrolyzes phosphatidylserine or lysophosphatidyl serine (LPS) specifically to produce GPS or Glycerol-3-P serine. LPS strongly enhances degranulation of rat mast cells induced by concanavalin A and potentiates histamine release, and can stimulate sPLA2-elicited histamine release from rat serosal mast cells. LPS is an inflammatory lipid mediator and sPLA2 has been implicated in inflammation processes. LPI has been shown to stimulate yeast adenylyl cyclase activity with implications for modulating the activity of downstream effector molecules and their interaction with RAS proteins.

Little is known about the mechanisms regulating LPA levels in vivo; however, the low LPA levels in plasma indicate that production, metabolism or clearance is tightly controlled. LPA is a normal phospholipid constituent of all cells and functions as a metabolic intermediate in de novo synthesis of glycerophospholipids and triglycerides. As with other lipid mediators like diacylglycerol and phosphoinositides, the relationship between this "housekeeping" LPA and LPA that exerts its actions through cell surface receptors in unclear. Clearly a growing variety of cells including platelets, adipocytes, leukocytes, fibroblasts, endothelial cells and, ovarian cancer cells, can release LPA into the extracellular space in response to agonist stimulation. Phospholipase A2

(PLA2)-mediated deacylation of phosphatidic acid (PA), produced by the action of phospholipase D (PLD) on membrane phosphatidylcholine (PC) or by the actions of diacylglycerol kinase on
A5 diacylglycerol formed by phospholipase C likely contributes to LPA production in response to cellular activation. The pathway for production of extracellular LPA has been most intensely studied in platelets where release of membraneous microvesicles is a critical step.

On page 33, line 4, please replace with the following paragraph:

The term "immobilized on a solid support" means that the nucleic acid polymer is bound, covalently or through an affinity reaction, to a relatively contiguous surface. The solid support may consist of any appropriate material for binding nucleic acids, including glass, silicas, hydrogels (such
A6 as agarose or polyacrylamide), polymers (such as polystyrene or polypropylene), and cellulose derivatives (such as nitrocellulose). The solid support may be in any convenient form for quantifying the amount of hybridization, including beads, resins, microtiter wells, flat surfaces, rods, and the like. For use in the arrays of the present invention, flat silicate surfaces, such as used in U.S. Patent No. 5,744,305, are preferred. Immobilization formats adapted to these surfaces have been developed which can be easily loaded with the lipid associated gene probe sequences described in the invention, and which can be easily read with automated equipment.